The opportunities for scientific discovery at the interface of the physical and biological sciences have attracted increasing attention over the past decade, evidenced by several insightful and comprehensive reports\textsuperscript{1,2,3,4,5} as well as a number of relatively new funding mechanisms (Appendix A). This 2010 symposium, jointly organized by the Burroughs Wellcome Fund, the W.M. Keck Foundation, and the Swartz Foundation, brought together key federal and private non-profit funders interested in exploiting these opportunities (See Appendix B for Agenda). The two day meeting highlighted current puzzles in biology\textsuperscript{6} from the perspective of different biological systems, chosen because of their potential to illuminate some common issues that cut across multiple levels of biological organization, and across multiple biological subfields. Cross-cutting themes for the sessions included variability, robustness, and homeostasis; adaptation and evolution; and signals, noise, and control. Speakers were asked to identify the ideas that currently generate significant excitement, as well as the obstacles that hinder pursuit of those questions. This summary highlights the ideas, issues, and solutions that arose during the symposium. It is not intended to be comprehensive, but rather, can form the basis for continued discussions on how to assemble the resources needed to capitalize on these opportunities.

A challenge presented by biological systems is that organisms are continuously rebuilding themselves while remaining functional. Understanding them requires simultaneously measuring system performance or behavior along with the underlying cellular and circuit parameters. Put another way, the challenge is understand the mechanisms and develop a theory of the dynamics occurring in constantly-changing living systems.

One recurring theme was the search for universal principles of network operation, with the recognition that network function is at the heart of biology, whether on the level of cell regulation, nervous systems, Darwinian systems, bacterial quorum sensing, social behavior, or ecosystems.

\textsuperscript{1} Research at the Intersection of the Physical and Life Sciences, Washington DC, The National Academies Press (2010).
\textsuperscript{6} There are also opportunities where biological approaches and perspectives may help solve puzzles in physics and engineering- but this was not addressed at this meeting.
Currently compelling questions include, but are not limited to these:

- How variable are the parameters in real biological networks, and how do the physiological and behavioral properties of the individual result from the particular parameter configurations?
- How much variability in behavior exists among genetically identical biological systems? In other words, what is the physics of the phenotypic diversity in genotypically identical organisms?
- How is function maintained during constant rebuilding in response to development or environmental change, and how can a full-scale network be monitored in real time as it functions? What are the laws governing the network dynamics?
- What is the structural and functional basis of network memory?

What is needed to address the challenges, both experimental and theoretical, at the interface of physics and biology?

- Tools for enabling multiscale and multipoint observations on a single system whether that is a neural circuit or an organ system
  - Engineering and biological expertise working in concert to improve/expand current technologies
  - Multimodal instruments including microscopy, spectral analysis and chemical/biochemical measurements
  - Include as many “omics” as possible
- Theory of open, nonlinear systems far from equilibrium
  - Statistical mechanics and dynamic systems theory are good starting points
  - Hardware and software innovations
  - Network analysis

How do we build an infrastructure to work toward meeting these challenges?

It boils down to supporting people and projects. For people, this includes shorter term experiences to engage investigators in new fields, as well as formal, multi-year training mechanisms. For projects, this will involve seed funding to test new ideas as well as longer term funding to sustain training programs and fund risky/high impact projects.

- Recruiting scientists to the interface
  - Develop mechanisms to support engagement at any stage of their careers of experts in mathematics, physics, computer science and biology to address life sciences questions, as well as to train biologists in physics and Mathematics. These will be different for graduate students, postdocs, independent early career scientists, mid career and senior scientists.
  - Support visiting scientist programs
- Support specific research projects
  - Support instrument, methods, technology development
  - Provide funds for shared technical experts in engineering and software/informatics that would be available to groups of scientists (Janelia Farm example)
  - Support high risk projects that would have a high impact

What other processes to facilitate the exchange of ideas are needed?

- Events: Conferences, workshops, short courses
  - Mathematical/statistical approaches for theorists
  - Instrument/methodology developers
- Social networks
- Ongoing forums
APPENDIX A:
FUNDING AGENCIES AND MECHANISMS Targeted to the Interface Between Physics and Biology

Burroughs Wellcome Fund
Career Awards at the Scientific Interface
www.bwfund.org

Howard Hughes Medical Institute
HHMI-NIBIB Interfaces Initiative for Interdisciplinary Graduate Research Training
www.hhmi.org
Janelia Farm
www.hhmi.org/janelia

The Kavli Foundation
www.kavlfoundation.org

W. M. Keck Foundation
Medical Research and Science and Engineering Research Awards
www.wmkeck.org/programs

Gordon and Betty Moore Foundation
www.moore.org/science.aspx

National Institutes of Health
National Cancer Institute
National Institute of Biomedical Imaging and Bioengineering
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke

See NIH Office of Extramural Research (OER) Extramural Training page:
grants.nih.gov/training/extramural.htm
Transforming Biomedicine at the Interface of the Life and Physical Sciences (PAR-10-141)
grants.nih.gov/grants/guide/pa-files/PAR-10-141.html
New Biomedical Frontiers at the Interface of the Life and Physical Sciences (PAR-10-142)
grants.nih.gov/grants/guide/pa-files/PAR-10-142.html
Physical Sciences - Oncology Centers (PS-OCs)
physics.cancer.gov
See NIBIB Extramural Training page:
Bioengineering Research Grants (PA-10-009)
grants.nih.gov/grants/guide/pa-files/PA-10-009.html
Bioengineering Nanotechnology Initiative (PA-10-150)
grants.nih.gov/grants/guide/pa-files/PA-10-150.html
Predictive Multiscale Models of the Physiome in Health and Disease (PAR-08-023)
grants.nih.gov/grants/guide/pa-files/PAR-08-023.html
BISTI: www.bisti.nih.gov/funding/index.asp

- Collaborative Research in Computational Neuroscience (CRCNS) (R01). A Joint NSF-NIH initiative: NSF-08-514
- Innovations in Biomedical Computational Science and Technology (R01, R21, SBIR, STTR)
- Continued Development and Maintenance of Software (R01) - PAR-08-010
- Predictive Multiscale Models of the Physiome in Health and Disease (R01) - PAR-08-023
- Collaborations with National Centers for Biomedical Computing (R01, R21)
- Data Ontologies for Biomedical Research (R01) - PAR-07-425
- Sharing Data and Tools: Federation using the BIRN and caBIG Infrastructures (R01) - PAR-07-426
- Neuroimaging Informatics Software Enhancement for Improved Interoperability and Dissemination (R03) - PAR-07-417
- Exceptional, Unconventional Research Enabling Knowledge Acceleration (EUREKA) (R01) - RFA-GM-10-009
- Bioengineering Research Partnerships (R01) - PAR-07-352
- Bioengineering Research Grants (R01) - PA-07-279
- Mentored Quantitative Research Development Award (K25) - PA-09-039
- Neuroscience Blueprint Computational Neuroscience Training Program (T90)

National Science Foundation
Physics of Living Systems (PoLS)
Biomolecular Systems Cluster
Collaborative Research in Computational Neuroscience
- www.nsf.gov/crcns
Cyber-enabled Discovery and Innovation
- www.nsf.gov/cdi
Integrative Graduate Education and Research Traineeship
- www.nsf.gov/crssprgm/igert/intro.jsp

Research Corporation for Science Advancement
Cottrell College Scholars and Scialog on Solar Conversion
- www.rescorp.org

Swartz Foundation
- www.theswartzfoundation.org

U.S. Department of Energy
Office of Biological and Environmental Research supports fundamental research for developing new methodologies for real-time, high-resolution imaging of dynamic biological processes in living systems including those of interest to DOE (e.g., biofuel plants and microbial communities).
- www.sc.doe.gov/ober/BSSD/radiochem.html
APPENDIX B: Meeting Agenda

Opportunities at the Interface of physics&biology

July 27-29, 2010

Four Seasons Hotel Chicago
120 E. Delaware, Chicago, IL 60611
(312) 280-8800

Tuesday, July 27, 2010

3:00 pm - 5:00 pm  Meeting Registration - State Room (8th Floor)
5:30 pm – 7:00 pm  Welcome Reception - Season’s Restaurant (7th Floor)

Wednesday, July 28, 2010

7:00 am – 8:30 am  Meeting Registration Continues – State Room (8th Floor)
7:30 am – 8:30 am  Breakfast - Delaware Room (7th Floor)
8:30 am – 8:45 am  Welcome and Introductions – State Room (8th Floor)
                  John Burris, Burroughs Wellcome Fund, Maria Pellegrini, W.M. Keck Foundation and Jerry Swartz, Swartz Foundation
8:45 am – 9:00 am  Overview of Meeting Goals
                  Nancy Sung (BWF), William Bialek (Princeton University) and Eve Marder (Brandeis University)
9:00 am – 11:50 am  Session 1 Variability, Robustness, and Homeostasis
                   Moderator: William Bialek
                   Aaron Dinner, University of Chicago: Signatures of Regulatory Synergies in Intrinsic Biological Noise
                   Mark Goldman, University of California-Davis: Robust Memories, Brittle Models: Challenges in Modeling Neural Activity in Short-term Memory Networks
                   Ned Wingreen, Princeton University: Why is the Vibrio harveyi Quorum Sensing Network So Complicated?
                   Marcelo Magnasco, Rockefeller University: Learning to be Critical
                   Eve Marder, Brandeis University: How Good is Good Enough in Neuronal Circuits and Behavior?
11:50 am – 12:30 pm  
**Open Discussion**

12:30 pm – 1:30 pm  
**Lunch** – Delaware Room (7th Floor)

1:30 pm – 3:15 pm  
**Session 2 Adaptation and Evolution** – State Room (8th Floor)  
*Moderator: Eve Marder*

Ralph Greenspan, UCSD/Kavli Neurosciences Institute: Does Biology Have Any Principles, Or Is It Just A Lot Of Stuff?


Michael Desai, Harvard University: How Do Large Populations Evolve?

Herb Levine, University of California-San Diego: Selection for Faster Adaptation

3:15 pm – 3:45 pm  
**Open Discussion**

3:45 pm – 4:00 pm  
**Break**

4:00 pm – 5:15 pm  
**Session 3 Signaling within boundaries** – State Room (8th Floor)  
*Moderator: William Bialek*

Boris Schraiman, U. California- Santa Barbara: Un-Expected Physics in Biology

Mary Kennedy, Caltech: Control of Synaptic Plasticity by Signaling in the Spine

Thierry Emonet Yale University: Spatial Regulation of Biological Function

5:15 pm – 6:00 pm  
**Open Discussion**

6:30 pm – 6:45 pm  
**Transportation to Field Museum**

7:00 pm – 10:00 pm  
**Reception and Dinner at Field Museum**

**Thursday, July 29, 2010**

8:00 am – 9:00am  
**Breakfast** – LaSalle Room (7th Floor)

9:00 am – 11:35 pm  
**Session 4 Signals, noise, and control** – State Room (8th Floor)  
*Moderator: Eve Marder*

Fred Rieke, University of Washington: Seeing in the Dark

Leslie Osborne, University of Chicago: Testing Theories of Optimality in Sensory-Motor Behavior

Emo Todorov, University of Washington: Optimal Control of Movement

William Bialek, Princeton University: How much can we calculate?

11:35 am – 12:30 pm  
**Open Discussion**

12:30 pm – 1:30 pm  
**Lunch** – LaSalle Room (7th Floor)
1:30 pm – 4:00 pm  
**Session 5: What is needed, and how do we get there?**
State Room (8th Floor)

This session will begin with a summary of the areas of opportunity identified by the talks earlier in the meeting, as a springboard for discussion of what is needed in the areas of training, tools, technology, and research funding. Funders will be asked to share their priorities as well as what they heard that is of interest.

**Confirmed Funders:**  
*John Burris, Burroughs Wellcome Fund*
*Nancy Sung, Burroughs Wellcome Fund*
*Maria Pellegrini, W.M. Keck Foundation*
*Jerry Swartz, Swartz Foundation*
*Hirsch Cohen, Swartz Foundation*
*Krastan Blagoev, NSF Physics of Living Systems Program*
*Richard Baird, NIH/NIBIB*
*Vicki Chandler, Gordon and Betty Moore Foundation*
*Miyounj Chun, Kavli Foundation*
*Richard Conroy, NIH/NIBIB*
*Martha Gilliland, Research Corporation for Science Advancement*
*Bill Galey, HHMI*
*Maryrose Franko, HHMI*
*Dennis Glanzman, NIH/NIMH*
*Yuan Liu, NIH/NINDS*
*Kevin Moses, HHMI/Janelia Farm*
*Larry Nagahara, NIH/NCI Physical Sciences- Oncology Center Program*
*David Thomassen, DOE*
*Renee Wegrzyn, DARPA*
*Kenneth Whang, National Science Foundation*

4:00 pm  
**Adjourn Meeting**